REMARKS

Status of the Claims

Claims 17, 34 and 52 are canceled without prejudice to future prosecution. Claims 8, 15, 16, and 18 are amended. Claims 124 to 137 are added. Therefore, claims 5-8, 11-16, 18-33, 35-51, 53-63, and 124-137 are pending after entry of this amendment.

Claim 8 has been amended to correct a typographical error. Claim 8 now recites "Q^3 is —OR^{28}" rather that " Q^3 —OR^{28}". Because the amendment merely corrects an obvious typographical error, no new matter is added with the amendment to claim 8.

Claims 15, 16, and 18 have been amended to delete the definitions of R^3 that are inconsistent with the definition of R^3 in claim 8. Therefore, no new matter is added with the amendments to claims 15, 16 and 18.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner asserts that the definition of R^3 in claims 15, 16, and 18 are inconsistent with the definition of R^3 in claim 8. Applicants agree and have deleted the inconsistent definitions in claims 15, 16, and 18. Therefore, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §112, second paragraph.

New Claims 124-131

Applicants respectfully request entry of claims 124-137. Applicants respectfully submit that new claims 124-137 each include common elements of the independent product claim 5. In addition, Applicants submit that the scope of claims 124-137 are not larger than the claim 5.

Claim 124

Claim 124 depends from claim 5 and, therefore, contains all of the limitations of claim 5. Claim 124 is no larger in scope than original claim 66. Applicants respectfully submit

that all of the terms of claim 124 are clear and well-supported in the specification. For example, on page 37, lines 22-30, the specification states:

> Examples of species to which the compounds of the invention can be conjugated include, for example, biomolecules such as proteins (*e.g.*, antibodies, enzymes, receptors, *etc.*), nucleic acids (*e.g.*, RNA, DNA, *etc.*), bioactive molecules (*e.g.*, drugs, toxins, *etc.*); solid subtrates such as glass or polymeric beads, sheets, fibers, membranes (*e.g.* nylon, nitrocellulose), slides (*e.g.* glass, quartz) and probes; *etc.*
> In a preferred embodiment, the species to which the compound is conjugated is a biomolecule. Preferred biomolecules are those selected from the group consisting of antibodies, nucleic acids, enzymes, haptens, carbohydrates and antigens.

In addition, Applicants submit that the terms antibodies, antigens, peptides, nucleic acids, enzymes, haptens, carbohydrates and pharmacologically active agents are well known in the art.

Methods of attaching the compound of claim 5 to antibodies, antigens, peptides, nucleic acids, enzymes, haptens, carbohydrates and pharmacologically active agents are discussed throughout the specification. For example, on page 25, lines 16-18, the specification discloses that polyethers may be used to attach the compound of claim 5 to various molecules and surfaces:

> In a still further preferred embodiment, one or more of the above-recited R groups is a polyether, preferably a member selected from ethylene glycol, ethylene glycol oligomers and combinations thereof, having a molecular weight of from about 60 daltons to about 10,000 daltons, and more preferably of from about 100 daltons to about 1,000 daltons . . . In another preferred embodiment, one or more of the above-recited R groups comprise a reactive group for conjugating said compound to a member selected from the group consisting of molecules and surfaces. Representative useful

> reactive groups are discussed in greater detail in the succeeding section. Additional information on useful reactive groups is known to those of skill in the art. *See*, for example, Hermanson, BIOCONJUGATE TECHNIQUES, Academic Press, San Diego, 1996.

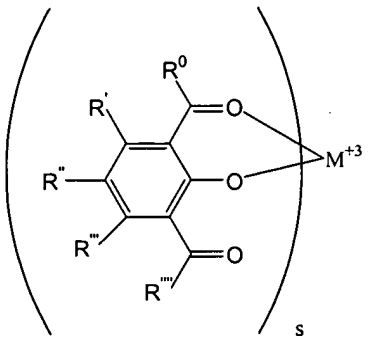
Claim 5 recites that R^1, R^2, R^4, R^5, R^6, R^7, R^{10} and R^{20} may be a polyether. Thus, after reading the disclosure above, one skilled in the art would immediately recognize that R^1, R^2, R^4, R^5, R^6, R^7, R^{10} or R^{20} may be attached to antibodies, antigens, peptides, nucleic acids, enzymes, haptens, carbohydrates and pharmacologically active agents using a reactive group. Reactive groups are discussed in detail in the "Reactive Functional Groups Section" of the specification from page 27, line 15 to page 29, line 9.

Therefore, Applicants respectfully request entry of claim 124.

Claims 125 and 129

Claim 125 depends from claim 5 and, therefore, contains all of the limitations of claim 5. Claim 125 is no larger in scope than original claim 71. Applicants respectfully submit that all of the terms of claim 125 are clear and well-supported in the specification. For example, on page 26, lines 6-9, the specification provides an exemplary structure of a metal ion coordinated to a compound of the present invention:

> Exemplary lanthanide chelates of the invention have a structure according to Structure 1:



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In addition, Applicants submit that the term lanthanide is well known in the art. Claim 129 depends from claim 125 and simply recites specific lanthanide metals. Therefore, Applicants respectfully request entry of claim 125.

Claims 126-128, and 130-131

Claims 126-128, and 130-131 depend from claim 125, which depends from claim 5. Therefore, claims 126-130 contain all the limitations of claim 5. Claims 126-128, and 130-131 are no larger in scope than original claims 68-70, and 71 respectively. Applicants respectfully submit that all of the terms of claims 126-128, and 130-131 are clear and well-supported in the specification. For example, on page 4, lines 8-10, the specification discloses luminescent complexes, as recited in claim 126: "The present invention provides lanthanide complexes that are extremely luminescent and possess many features desired for fluorescent markers and probes of use in fluorescent assay systems."

On page 14, lines 3-7, the specification discloses complexes that emit luminescence electrochemically and emit circularly polarized luminescence, as recited in claims 128 and 127, respectively:

> The compounds of the invention can be made to luminesce by exciting them in any manner known in the art, including, for example, with light or electrochemical energy (*see*, for example, Kulmala *et al, Analytica Chimica Acta* **386**: 1 (1999)). The luminescence can, in the case of chiral compounds of the invention, be circularly polarized (*see*, for example, Riehl *et al., Chem. Rev.* **86**: 1 (1986)).

On page 72, lines 12-25, the specification discloses substrates for the transmission and amplification of light, as recited in claims 130 and 131:

> [O]ptical fiber amplifiers have recently been developed, *i.e.* amplifiers which amplify the optical signal directly and do not need a conversion into an electrical signal. Such devices are disclosed in, for example, Yan *et al.*, U.S. Patent No. 5,982,973, issued November 9, 1999; Kleinerman, U.S. Patent No. 5,928,222, issued July 27,

> 1999; Desurvire, *Physics Today*, January 1994, 20-27; Sloof *et al., J. Appl. Phys.* **83**: 497 (1998).
> Thus, in another embodiment, the present invention provides a substrate for the transmission and amplification of light, said substrate comprising a compound of the invention. The compound of the invention can be incorporated into the substrate in any manner known in the art, including, but not limited to, covalent attachment, coating, doping, and the like any material useful for a particular application, including, but not limited to, glass, organic polymers, inorganic polymers and combinations thereof.

Therefore, Applicants respectfully request entry of claims 126-128, and 130-131.

New Claims 132-137

Claims 132-137 are method claims that depend from claim 125, which includes each limitation of the independent product claim 5. Applicants respectfully direct the Examiner's attention to M.P.E.P § 821.04, which states "...if Applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all of the limitations of the allowable product claim will be rejoined." Applicants respectfully request that if claim 125 is entered, that claims 132-137 be entered in accordance with M.P.E.P § 821.04.

Applicants respectfully submit that the terms of claims 132-137 are clear and well-supported by the specification. For example, the term "quencher of light energy" in claims 132-136, is explained in detail in the "Donor and Acceptor Moieties" section of the specification (page 29, line 10 to page 34, line 29). Guidance in choosing quenchers is provided, for example, on page 32, lines 1-11:

> [I]t is generally preferred that an absorbance band of the acceptor substantially overlap a fluorescence emission band of the donor. When the donor (fluorophore) is a component of a probe that utilizes fluorescence resonance energy transfer (FRET), the donor fluorescent moiety and the quencher (acceptor) of the invention are preferably

> selected so that the donor and acceptor moieties exhibit fluorescence resonance energy transfer when the donor moiety is excited. One factor to be considered in choosing the fluorophore-quencher pair is the efficiency of fluorescence resonance energy transfer between them. Preferably, the efficiency of FRET between the donor and acceptor moieties is at least 10%, more preferably at least 50% and even more preferably at least 80%. The efficiency of FRET can easily be empirically tested using the methods both described herein and known in the art.

In addition, the specification provides guidance in "detecting said change in said fluorescence parameter." For example, on page 34, lines 23-29, the specification discloses:

> Means of detecting fluorescent labels are well known to those of skill in the art. Thus, for example, fluorescent labels can be detected by exciting the fluorophore with the appropriate wavelength of light and detecting the resulting fluorescence. The fluorescence can be detected visually, by means of photographic film, by the use of electronic detectors such as charge coupled devices (CCDs) or photomultipliers and the like. Similarly, enzymatic labels may be detected by providing the appropriate substrates for the enzyme and detecting the resulting reaction product.

Claims 132-137 recite methods using oligonucleotides or peptides comprising the complex of claim 125. The specification provides extensive guidance for attaching complexes to oligonucleotides and/or peptides. For example, on page 33, line 12 to page 34, line 22, which states in part:

> Those of skill in the art will appreciate that the complexes of the invention can also be attached to small molecules (*e.g.*, small molecular bioactive agents), proteins, peptides, synthetic polymers, solid supports and the like using standard synthetic chemistry or modifications thereof . . .
> In view of the well-developed body of literature concerning the conjugation of small molecules to nucleic acids, many other methods of attaching donor/acceptor pairs to nucleic acids will be apparent to those of skill in the art. For example, rhodamine and fluorescein dyes are conveniently attached to the 5'-hydroxyl of an nucleic acid at the

> conclusion of solid phase synthesis by way of dyes derivatized with a phosphoramidite moiety (*see*, for example, Woo *et al.*, U.S. Pat. No. 5,231,191; and Hobbs, Jr., U.S. Pat. No. 4,997,928).
>
> More specifically, there are many linking moieties and methodologies for attaching groups to the 5'- or 3'-termini of nucleic acids, as exemplified by the following references: Eckstein, editor, Nucleic Acids and Analogues: A Practical Approach (IRL Press, Oxford, 1991); Zuckerman *et al.*, *Nucleic Acids Research*, **15**: 5305-5321 (1987) (3'-thiol group on nucleic acid); Sharma *et al.*, *Nucleic Acids Research*, **19**: 3019 (1991) (3'-sulfhydryl); Giusti *et al.*, *PCR Methods and Applications*, **2**: 223-227 (1993) and Fung *et al.*, U.S. Pat. No. *4,757,141* (5'-phosphoamino group via Aminolink TM II available from P.E. Biosystems, CA.) Stabinsky, U.S. Pat. No. 4,739,044 (3-aminoalkylphosphoryl group); Agrawal *et al.*, *Tetrahedron Letters*, **31**: 1543-1546 (1990) (attachment via phosphoramidate linkages); Sproat *et al.*, *Nucleic Acids Research*, **15**: 4837 (1987) (5-mercapto group); Nelson *et al.*, *Nucleic Acids Research*, **17**: 7187-7194 (1989) (3'-amino group), and the like.

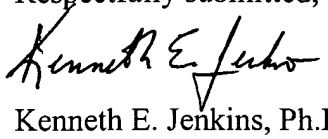
In addition, reactive functional groups useful for attaching complexes to nucleic acids and/or peptides are discussed in the specification in the "Reactive Functional Groups Section" from page 27, line 15 to page 29, line 9.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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